REMARKS

All pending claims are now consistent with the elected subject matter following the amendments above. In making these amendments, Applicants do not concede there is any basis for the restriction requirement.

Claims 29, 30, 36 and 48 have been amended to identify certain cancers described on page 2, lines 12-22 of the specification. Applicants maintain the specification provides a sufficient written description of the subject matter within the original claims and the claims as amended to satisfy the statute. In making these amendments, Applicants do not concede there is any merit to the rejections under 35 USC §112.

Restriction/Election

Applicants have never taken the position that the restricted subject matter is not patentably distinct and they have not traversed the restriction requirement on such grounds. Instead, applicants have traversed the restriction requirement on the basis that no evidence has been presented that it would be an undue burden to search the full scope of the claimed subject matter. Applicants have identified common features such as the required substituents on L^1 (SO_2R_x, $C(O)R_x$ and $C(NR_y)R_z$) which should narrow the search.

Rejections Under 35 U.S.C. § 112

The rejection of claims 1-22, 24-30, 34-37,39,40,42,45-48 under 35 USC §112 is moot following the amendments above conforming the claims to the elected group. Applicants maintain that the specification provides adequate disclosure to satisfy all the requirements under 35 USC §112 for the subject matter of both the original claims and the claims as amended.

The specification provides both general and specific methods for making compounds consistent with formula I and both dosages and methods of administering these compounds are given within the specification. Some experimentation may be required to make and use compounds which have not been exemplified but there is no evidence this experimentation would be undue. In the absence of such evidence, all claims must be taken to satisfy the requirements of 35 U.S.C. § 112, first paragraph.

The specification provides a number of publications which have correlated the inhibition of raf kinase with the inhibition of the growth of a variety of tumor types (Monia et al.), correlated the inhibition of raf expression with blocking cell proliferation (Kolch et al.) or correlated the inhibition of the raf kinase pathway with the reversion of transformed cells to the normal growth phenotype (Daum et al., Fridman et al).

No evidence has been presented to refute the findings or conclusions made in these publications. In addition, no evidence has been presented that any compounds of this invention, as inhibitors of raf kinase, would not be effective in treating the cancers identified. Only unsupported allegations and conclusions regarding the art of cancer treatment are provided to support the rejection.

In any event, the specification also otherwise provides ample guidance as to how to prepare pharmaceutical compositions with the compounds of this invention and how to administer these compositions in the treatment of cancers. See, e.g., pages 16-21. The specification also provides dosage ranges for the various methods of administration (see page 20). Given the extent of the disclosure provided, it would at most involve routine experimentation if any at all, for one of ordinary skill in the art to treat any one of the recited cancers with a compound of this invention.

Even absent the specification disclosures discussed above, the rejection is clearly deficient in general under controlling case law. The courts have placed the burden upon the PTO to provide evidence shedding doubt on the disclosure that the invention can be made and used as stated; see, e.g., *In re Marzocchi*, 439 F.2d 220, 169 U.S.P.Q. 367 (CCPA 1971) (holding that how an enablement teaching is set forth, either by use of illustrative examples or by broad terminology, is of no importance.) The disclosure must be taken as in compliance with the enablement requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein. See *In re Marzocchi*, supra. No such evidence or reason for doubting Applicants' disclosure has been provided. Only general statements and conclusions are made.

Additionally, "the [enablement] requirement is satisfied if, given what they [, those of ordinary skill in the art,] already know, the specification teaches those in the art enough that they can make and use the claimed invention without 'undue experimentation.'" See *Amgen v Hoechst Marion Roussel*, 314 F.2d 1313, 65 USPQ2d 1385 (Fed. Cir. 2003). Using the

claimed compounds would be routine for those of ordinary skill in the art in view of applicant's disclosure. See, for example, *In re Howarth,* 654 F.2d 105, 210 U.S.P.Q. 689 (CCPA 1981) ("An inventor need not ... explain every detail since he is speaking to those skilled in the art."); *In re Gay*, 309 F.2d 769, 774, 135 U.S.P.Q 311 (CCPA 1962) ("Not every last detail is to be described, else patent specifications would turn into production specifications, which they were never intended to be.")

There is no requirement that an applicant provide any working examples relating to the treatment of every claimed disease to satisfy the statute. See, for example, *Marzocchi*, supra, stating that how "an enabling teaching is set forth, either by use of illustrative examples or by broad terminology, is of no importance." The MPEP also agrees by stating that "compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is disclosed." See MPEP § 2164.02.

The PTO has failed to meet its burden of establishing that the disclosure does not enable one skilled in the art to make and use the compounds recited in the claims. Moreover, with respect to pharmaceutical inventions, an applicant is not required to test the claimed compounds in their final use (rigorous planned and executed clinical trials..." per the Examiner). The Federal Circuit in *In re Brana*, 51 F.3d 1560, 34 USPQ 1436 (Fed. Cir. 1995), stated that:

> usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful can be well before it is ready to be administered to humans. If the courts were to require Phase II testing in order to prove utility for pharmaceutical inventions, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas.

Here, the specification provides more than it needs to, e.g, *in vitro* raf kinase assays (and IC_{50} data) and *in vivo* assays (see pages 105 and 106). In similar fashion, one of

ordinary skill in the art by performing the same or similar tests, can, by routine experimentation, determine the activity levels of each of the claimed compounds in treating various cancers. This is absolutely routine in the field.

For the reasons discussed above, Applicants submit that all pending claims meet the requirements of 35 U.S.C. § 112, first paragraph.

Rejection Under 35 U.S.C. § 112, second paragraph

The rejection of claims 29, 30, 36 and 48 under 35 U.S.C. § 112, second paragraph, is moot following the amendments above. Applicants maintain that there is adequate written description within the specification of the subject matter defined by all original claims, including the treatment of diseases defined by the functional language used in original claims 29, 30, 36 and 48.

Applicants also maintain that there is clearly adequate written description of the conditions to be treated described on page 2 of the specification and in amended claims 29, 30, 36 and 48.

Double Patenting

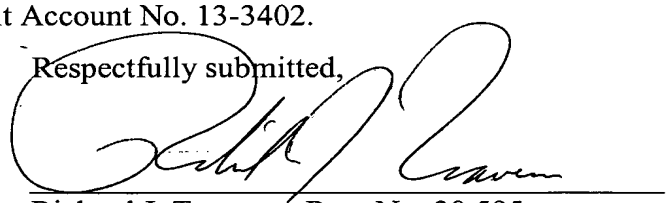
Applicants submit the subject matter claimed herein is not obvious in view of the subject matter claimed in copending application 10/788,029 in that the compounds defined in these claims are structurally distinct. For example, the compounds claimed herein require that the moiety L^1 have at least one substituent selected from the group consisting of $-SO_2R_x$, $-C(O)R_x$ and $-C(NR_y)R_z$, (which is not required of the compounds claimed in Application No. 10/788,029) and the compounds claimed in Application No. 10/788,029 require that the moiety corresponding to L^1 have a cyano group. There are similar structural distinctions between the compounds claimed herein and the cyano substituted urea (ZB) identified in Application No. 10/848,567. The other urea (ZC) identified in Application No. 10/848,567 does not have a pyridine ring structure for the moiety corresponding to "B" of formula I.

The claimed compounds are also structurally distinct form those claimed in Application No. 10/361,858 in that they do not require one of the conditions a-c defined by the proviso in claim 1 of Application No. 10/361,858. In view of the structural distinctions described above, applicants maintain there is no basis for the obviousness-type double patenting rejections.

Based on the above remarks, applicants submit that pending claims are in condition for allowance.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



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